CSP

Alterations in left ventricular torsion in tachycardia-induced dilated cardiomyopathy

Frederick A. Tibayan, MD[a]
David T. M. Lai, FRACS[a]
Tomasz A. Timek, MD[a]
Paul Dagum, MD, PhD[a]
David Liang, MD, PhD[b]
George T. Daughters, MS[a,c]
Neil B. Ingels, PhD[a,c]
D. Craig Miller, MD[a]

Objective: Left ventricular torsion reduces transmural systolic gradients of fiber strain, and torsional recoil in early diastole is thought to enhance left ventricular filling. Left ventricular remodeling in dilated cardiomyopathy may result in changes in torsion dynamics, but these effects are not yet characterized. Tachycardia-induced cardiomyopathy is accompanied by systolic and diastolic heart failure and left ventricular remodeling. We hypothesized that cardiomyopathy would alter systolic and diastolic left ventricular torsion mechanics, and this hypothesis was tested by studying sheep before and after the development of tachycardia-induced cardiomyopathy.

Methods: Implanted miniature radiopaque markers were used in 8 sheep to measure left ventricular geometry and function, maximal torsional deformation, and early diastolic recoil before and after rapid ventricular pacing was used to create tachycardia-induced cardiomyopathy.

Results: All animals had significant heart failure with ventricular dilatation and remodeling. With tachycardia-induced cardiomyopathy, maximum torsion relative to control conditions decreased (1.69° ± 0.61° vs 4.25° ± 2.33°), and early diastolic recoil was completely abolished (0.53° ± 1.19° vs −1.17° ± 0.94°).

Conclusions: Cardiomyopathy is accompanied by decreased and delayed systolic left ventricular torsional deformation and loss of early diastolic recoil, which may contribute to left ventricular dysfunction by increasing systolic transmural strain gradients and impairing diastolic filling. Analysis of left ventricular torsion with radiofrequency-tagging magnetic resonance imaging should be explored to elucidate the role of torsion in patients with cardiomyopathy.

From the Department of Cardiovascular and Thoracic Surgery,[a] Division of Cardiovascular Medicine,[b] Stanford University School of Medicine, Stanford, Calif, and the Laboratory of Cardiovascular Physiology and Biophysics,[c] Research Institute of the Palo Alto Medical Foundation, Palo Alto, Calif.

Supported by grants HL-29589 and HL-67025 from the National Heart, Lung, and Blood Institute. Drs Tibayan, Lai, Timek, and Dagum are Carl and Leah McConnell Cardiovascular Surgical Research Fellows. Dr Timek is a recipient of the Thoracic Surgery Foundation Research Fellowship. Drs. Timek, Dagum, and Tibayan were supported by NHLBI Individual Research Service Awards HL-10452, HL-09569, and HL-67563, respectively. Dr Lai was supported by a fellowship from the American Heart Association, Western States Affiliate.

Received for publication Aug 8, 2001; revisions requested Sept 17, 2001; revisions received Oct 12, 2001; accepted for publication Oct 24, 2001.

Address for reprints: D. Craig Miller, MD, Department of Cardiovascular Surgery, Falk Cardiovascular Research Center, Stanford University School of Medicine, Stanford, CA 94305-5247 (E-mail: dcm@leland.stanford.edu).

J Thorac Cardiovasc Surg 2002;124:43-9

0022-5223/2002 $35.00+0 **12/1/121299**

doi:10.1067/mtc.2002.121299

Contraction of the helically oriented fibers in the left ventricle[1,2] results in torsion, a wringing motion as the apex rotates with respect to the base about the left ventricular (LV) long axis.[3,4] Torsion is thought to play an important role in decreasing gradients of LV transmural fiber strain and oxygen demand during systole,[5,6] and torsion recoil during diastole has been hypothesized to aid ventricular filling.[7] Dilated cardiomyopathy is associated with LV remodeling (dilatation, wall thinning, and, possibly, reduction in fiber angles) that may alter torsion and its beneficial effects. Surgical approaches for patients with dilated cardiomyopathy, ischemic cardiomyopathy, or both, such as the surgical anterior ventricular endocardial restoration procedure, may improve LV systolic function by restoring normal ventricular shape, fiber angle, and torsional mechanics[8,9]; however, the effects of cardiomyopathy on LV torsion dynamics have not been characterized.

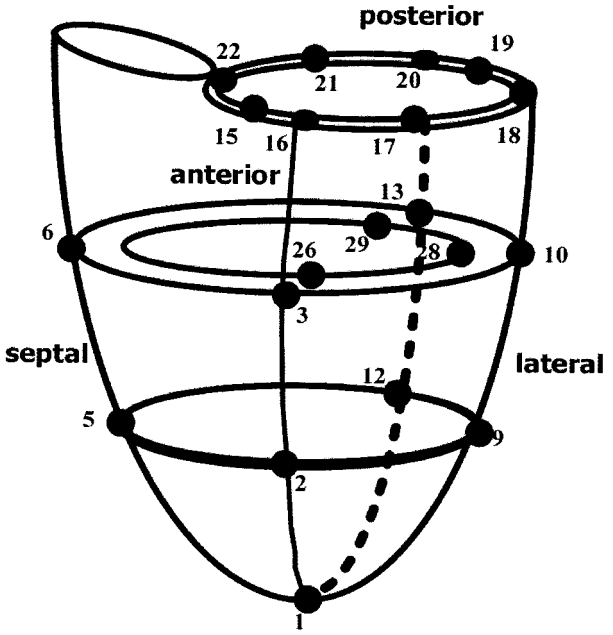

Figure 1. Schematic representation of myocardial marker array used in this study.

Tachycardia-induced cardiomyopathy (TIC), a model of dilated cardiomyopathy, is accompanied by ventricular remodeling, systolic and diastolic dysfunction,[10] and neurohumoral changes[11] similar to the clinical entity. We hypothesized that such changes would result in alterations of systolic and diastolic LV torsion dynamics and tested this hypothesis by measuring the 3-dimensional (3-D) dynamics of implanted radiopaque LV markers in sheep before and after the development of TIC.

Methods

Surgical Preparation

Radiopaque markers were implanted into the hearts of 8 adult sheep. The technical details have been previously described[12] and will only be summarized briefly. Eight tantalum helices were inserted in the LV epicardial layer at 2 LV levels along 4 equally spaced longitudinal meridians (nos. 2, 3, 5, 6, 9, 10, 12, and 13; Figure 1), with one marker placed at the LV apex (no. 1) and subendocardial markers 26, 28, and 30 paired opposite subepicardial markers 3, 10, and 13, respectively. On cardiopulmonary bypass, 8 markers (nos. 15-22) were sutured around the circumference of the mitral anulus. A micromanometer pressure transducer was placed in the LV chamber through the apex. A monopolar pacing lead was sewn onto the anterior LV wall.

Data Acquisition

After 6 ± 1 days, each animal was taken to the experimental cardiac catheterization laboratory, sedated with ketamine (1-4 $mg \cdot kg^{-1} \cdot h^{-1}$ intravenous infusion) and diazepam (5 mg intravenous bolus as needed), intubated, and mechanically ventilated. With the animal in the right lateral position, simultaneous biplane videofluoroscopic images were acquired at 60 Hz. The images were digitized and merged to yield the 3-D coordinates for each marker every 16.7 ms with custom-designed software. Synchronized ascending thoracic aortic pressure, LV pressure, and electrocardiographic analog signals were digitized and recorded simultaneously during videographic data acquisition. An experienced echocardiographer (D.L.) used transesophageal Doppler echocardiography to assess mitral regurgitation.

Rapid-pacing Protocol

After baseline data acquisition, a rapid-pacing pulse generator (Prodigy S 8164; Medtronic Inc, Minneapolis, Minn) was inserted subcutaneously and connected to the monopolar LV electrode. Rapid pacing was initiated 24 hours later. During the pacing period, transthoracic echocardiography was performed every 2 to 3 days to assess LV dimensions and systolic LV performance (with the pacer temporarily off). Pacing was continued until development of TIC, as evidenced by development of peripheral edema, ascites, and/or increase in end-systolic LV dimension. The first 2 animals were paced at a rate of 180 min^{-1}, and subsequent animals were paced at 230 min^{-1}, which resulted in faster development of heart failure. The average pacing period was 15 ± 6 days. Then the animals were returned to the catheterization laboratory, with the pacer turned off immediately before data acquisition. Hemodynamic, marker, and echocardiographic data were again acquired, as described above.

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (DHEW NIHG publication no. 85-23, revised 1985). This study was approved by the Stanford Medical Center Laboratory Research Animal Review Committee and conducted according to Stanford University policy.

Data Analysis and Computation of LV Torsion

Values computed from 3 consecutive steady-state beats during normal sinus rhythm before and after TIC were averaged and labeled as "control" and "TIC" data for each animal. Instantaneous LV volume (LLV) was calculated from the epicardial LV markers by using a space-filling multiple tetrahedral volume method every 16.7 ms.[13] End-diastole (ED) was defined as the time of the peak of the electrocardiographic R-wave, end-ejection as the time of minimum LVV, and end-systole (ES) as the time of peak negative rate of LV pressure decrease ($-dP/dt$). Stroke volume (SV) was calculated as the difference between end-diastolic volume (EDV) and minimum LVV (LVV_{min}; $SV = EDV - LVV_{min}$).

At each sample time, all marker Cartesian 3-D coordinates (x, y, and z) were transformed into a moving internal cylindrical coordinate system (r, φ, and z) with the origin at the centroid of the annular markers (markers 15-22, Figure 1), the z-axis passing through the centroid of the markers defining the apical transverse LV plane (markers 2, 5, 9, 12), the 0° reference passing through the anterior commissure (marker 16), and positive angles defined as counterclockwise when looking from apex to base.

For each apical-level epicardial marker (nos. 2, 5, 9, and 12; Figure 1), the circumferential rotational angle (φ) change relative

to ED was computed throughout the cardiac cycle. In each frame torsion was defined as the average angular displacement of the apical markers on the free walls of the ventricle, and data from 3 consecutive steady-state beats were averaged. As viewed from the LV apex, with positive angles counterclockwise, during beat b (from ED_b to ED_{b+1}), the torsional deformation Φ at each sample time t ($=0@ED_b$, 1, 2, . . ., $t@ED_{b+1}$) of marker m subtending angle $\varphi_m(t)$ was computed as follows:

$$\Phi_m(t) = \varphi_m(t) - \varphi_m(ED_b) \quad (1)$$

Mean free-wall LV torsional deformation ($\psi_b[t]$) for beat b was then computed as follows:

$$\psi_b(t) = [\Phi_2(t) + \Phi_9(t) + \Phi_{12}(t)]/3 \quad (2)$$

and mean free-wall LV torsional deformation for the 3-beat sequences comprising each run in each heart as follows:

$$\Phi(t) = [\psi_1(t) + \psi_2(t) + \psi_3(t)]/3 \quad (3)$$

Fractional ejection at each sample time (t) for each beat (b) was defined as follows:

$$FRAC_b(t) = [LVV_{EDVb} - LVV_b(t)]/(LVV_{EDVb} - LVV_{EEb}) \quad (4)$$

where $LVV_b(t)$ is LVV at time t, LVV_{EDVb} is LVV at EDV, and LVV_{EEb} is LVV at end-ejection for beat b. Mean fractional ejection at each sample time (t) for the 3-beat sequences comprising each run in each heart was as follows:

$$FRAC(t) = [FRAC_1(t) + FRAC_2(t) + FRAC_3(t)]/3 \quad (5)$$

Figure 2 illustrates mean free-wall torsional deformation $\Phi(t)$ plotted against FRAC(t) for both control and TIC conditions in a representative animal. $\Phi(t)$ was characterized by minimum free-wall LV torsional deformation during early systole (Φ_{min}), maximum free-wall LV torsional deformation, typically occurring near ES (Φ_{max}), and absolute value of change in free-wall torsional deformation from end ejection to the first 5% of LV filling ($\Phi_{5\%}$) to assess early diastolic torsional recoil.[7] Time of Φ_{max} relative to end ejection ($T_{\Phi maxEE}$), was also calculated.

Statistical Analysis

All data are reported as means ± 1 SD. Data were compared with the Student *t* test for paired observations.

Results

Hemodynamics

Table 1 summarizes the hemodynamic variables measured before and after development of TIC. Cardiomyopathy was associated with a significant increase in LV end-systolic (+30%, $P = .0001$) and end-diastolic (+24%, $P = .0004$) volume and a significant reduction (−30%, $P = .03$) in preload recruitable stroke work. Heart rate (+17%, $P = .04$) and LV end-diastolic pressure (+81%, $P = .01$) were also significantly higher with cardiomyopathy. Before pacing, the animals had zero to trace mitral regurgitation (average = 0.2 ± 0.3 on a scale from 0 to +4; 0 = none, 1 = trace, 2 = mild, 3 = moderate, and 4 = severe); after development of TIC, the mitral regurgitation grade increased significantly to 2.2 ± 0.9 ($P = .0001$).

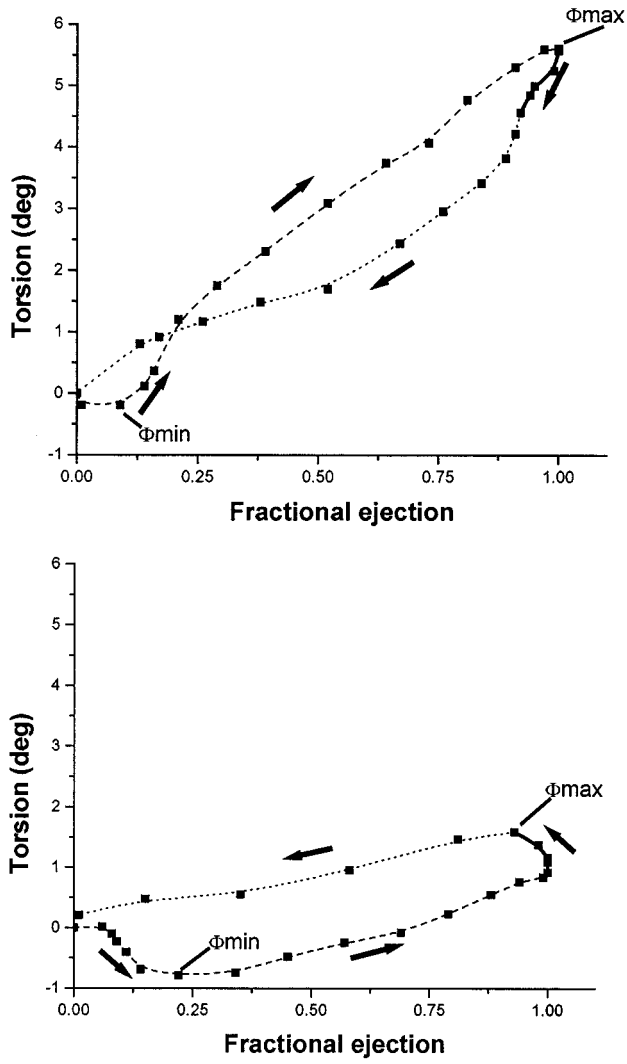

Figure 2. Torsion (Φ[t]) versus fractional ejection (FRAC[t]) under control *(above)* and TIC *(below)* conditions in a representative animal. In control conditions systole *(dashed line)* is characterized by a slight clockwise rotation (negative deflection), followed by counterclockwise torsion that peaks at end-ejection. Early diastole *(solid line)* shows more rapid torsional recoil than mid-to-late diastole *(dotted line)*. After development of cardiomyopathy, the clockwise deformation is larger, and the maximum positive torsion is decreased. Moreover, this peak is reached after end-ejection. Accordingly, there is loss of torsional recoil in early diastole.

LV Torsion Mechanics

As shown in Figure 2, under control conditions, systole began with a small negative (ie, clockwise, as viewed from apex) torsional deformation. After this cocking twist, a relatively linear direct relationship between torsion and

TABLE 1. Hemodynamics

	Control	TIC	*P* value
HR (min^{-1})	101 ± 16	118 ± 20	.04
LV dP/dt (mm Hg/s)	1365 ± 282	1212 ± 437	.23
LV EDV (mL)	175 ± 18	217 ± 27	.0004
LV ESV (mL)	138 ± 17	180 ± 23	.0001
LVEDP (mm Hg)	16 ± 7	29 ± 10	.01
LVPmax (mm Hg)	95 ± 18	94 ± 17	.48
PRSW (mm Hg)	63 ± 14	44 ± 12	.03

Data shown as means ± 1 SD. *HR*, Heart rate; *LV dP/dt*, maximum positive rate of change of LV pressure; *LV ESV*, LV end-systolic volume; *LVEDP*, LV end-diastolic pressure; *LVPmax*, maximum systolic LV pressure; *PRSW*, LV preload recruitable stroke work.

TABLE 2. LV torsion measurements

	Control	TIC	*P* value
Φ_{min} (°)	−0.67 ± 0.67	−1.51 ± 3.80	.004
Φ_{max} (°)	4.25 ± 2.33	1.69 ± 0.61	.007
$\Phi_{5\%}$ (°)	−1.17 ± 0.94	−0.53 ± 1.19	.01
$T_{\Phi maxEE}$ (msec)	−42 ± 30	71 ± 72	.005

Data shown as means ± SD. Φ_{min}, Minimum early systolic negative torsion; Φ_{max}, maximum positive torsion; $\Phi_{5\%}$, absolute change in torsion during isovolumic relaxation and early diastole (end-ejection through 5% filling); $T_{\Phi maxEE}$, time (ms) of Φ_{max} relative to end-ejection (negative = before end-ejection; positive = after end-ejection).

ejected volume was observed during the majority of systole until Φ peaked just before end-ejection. Isovolumic relaxation (IVR) and early diastole (defined as the interval from end-ejection through the first 5% of ventricular filling) were characterized by abrupt torsional recoil (ie, a decrease in Φ), followed by more gradual untwisting during mid and late diastole. With dilated cardiomyopathy, the initial early systolic negative cocking torsion was larger and more sustained, and Φ_{max} was reduced, as well as delayed until after the time of end-ejection, such that Φ was still increasing during IVR and early diastole.

Table 2 summarizes torsion dynamics before and after the development of cardiomyopathy. In the cardiomyopathic state, as compared with control conditions, early systolic clockwise (negative) torsion (Φ_{min}) increased significantly, Φ_{max} decreased significantly, and early diastolic recoil was abolished, as indicated by the change in sign of $\Phi_{5\%}$ from negative (clockwise) in control to positive (continued counterclockwise torsion) in TIC conditions. In control conditions Φ_{max} occurred 42 ± 30 ms before end-ejection; however, Φ_{max} was reached considerably after end-ejection (71 ± 72 ms) in the cardiomyopathic conditions.

Discussion

TIC markedly changes LV torsional mechanics throughout the cardiac cycle. Although the initial clockwise cocking rotation in early systole (Φ_{min}) was greater in amplitude in the cardiomyopathic state, maximal torsional deformation (Φ_{max}) was significantly reduced. It is thought that systolic torsion is a mechanism by which the ventricle equilibrates transmural gradients of fiber strain and oxygen demand.[5,6,14-16] Using computer models, others have demonstrated that LV systolic torsion may lower subendocardial oxygen demand[17] and increase subendocardial blood flow.[18] Thus when systolic LV torsion is reduced, as in cardiomyopathic hearts, the fiber-strain gradients and metabolic gradients across the LV wall would be expected to be larger, with greater subendocardial oxygen requirement. Indeed, animal models suggest that an imbalance of oxygen supply and demand plays a role in the pathophysiology of TIC, with the perfusion deficit being greatest in the subendocardial layers.[19,20] Decreased torsion may cause the ventricle to lose its ability to modulate these transmural metabolic gradients, thereby contributing to or exacerbating the imbalance of oxygen supply and demand.[21]

In the present study Φ_{max} was not only reduced, but it was also delayed in the cardiomyopathic conditions compared with in the control state. Before pacing, Φ_{max} occurred slightly before or at the time of end-ejection, but with cardiomyopathy, Φ_{max} was delayed until after end-ejection. This suggests that not only is the ventricle less capable of equalizing transmural work and metabolic gradients but also that such equalization was not fully effective until after systolic force generation had peaked. Kroeker et al[22] reported that maximal torsional deformation was delayed into IVR in a canine model of acute LV ischemia and postulated that this might affect the release of restoring forces and thereby impair early filling of the ventricle.

The cardiomyopathic dilated hearts also had marked alterations in diastolic LV torsional dynamics. Studies of normal dogs[7,23] and human patients[24] indicate that the bulk of LV torsional recoil occurs during IVR. In the present study, during IVR and the first 5% of diastolic LV filling, a rapid untwisting or torsional recoil was seen during control conditions. With cardiomyopathy, this early diastolic recoil was lost, and torsion actually continued to increase slightly during this period. Early diastolic recoil represents rapid release of LV-restoring forces (potential energy) stored in the extracellular matrix and contractile elements during systole.[25,26] In turn, early diastolic recoil might play a role in the genesis of LV suction and enhance LV early diastolic filling.[7,22] Stuber and coworkers[24,27] suggested that delayed untwisting in patients with aortic stenosis and coronary artery disease could contribute to diastolic LV dysfunction. In a canine model of pacing-induced tachycardia, Bell and colleagues[23] recently reported a decrease in the rate of torsional recoil, which corresponded to a loss of the determinants of LV diastolic suction. Therefore the loss of early diastolic recoil with cardiomyopathy, as observed in the

present study, could theoretically adversely affect LV filling and diastolic suction.

In addition to alterations in torsion dynamics, rapid pacing caused significant hemodynamic changes. Cardiomyopathy was evidenced by peripheral edema, ascites, lethargy, ventricular dilatation, increased LV end-diastolic pressure, and reduced preload recruitable stroke work, a load-independent measure of contractility. Contractility has a direct effect on torsion independent of loading conditions.[28,29] Therefore decreased contractility might contribute to a reduction of Φ_{max} in TIC because it is the shortening of the myofibers that drives the torsional deformation. Dilatation may play a part in the alterations in torsion by equalizing the lengths of the opposing lever arms that give rise to torsion (vide infra). Although other investigators of TIC have noted decreased maximum LV pressure and dP/dt, these load-dependent measures were unchanged in the present study. Because the degree of cardiomyopathy in TIC is related to the intensity and length of pacing,[30] such differences may be accounted for by a faster rate,[31,32] a longer period of pacing,[10,32] or species differences.

The mechanisms underlying the changes in torsion dynamics are unknown but probably encompass many factors, including remodeling of the cardiomyocytes and connective tissue matrix, slowed transmural fiber activation, and alterations in excitation-contraction coupling. First, LV dilatation accompanies TIC, as observed in this study and reported by others.[31,33] To see how this might affect torsion, consider that, at a given instant, the net moment giving rise to torsion can be thought of as a sum (resultant) of the opposing circumferential moments (vectors) of the LV subendocardium and the subepicardium. Ingels and coworkers[34] proposed several factors that influence the magnitude and direction of these vectors: fiber orientation, number of fibers, and lengths of the lever arms of the respective layers. Thus although the angles of inclination of the subendocardial and subepicardial fibers are roughly equal (but opposite in sign), physiologic torsion during systole is dominated by the subepicardial fibers caused by their larger radii. Both ventricular dilatation and wall thinning tend to equalize the radii of the subendocardial and subepicardial layers, thus allowing a relatively greater contribution from the subendocardium to the net torsion moment. In a model examining the effects of ventricular geometry on torsion, Taber et al[14] predicted such a result by reasoning that in eccentric hypertrophy the epicardial fibers would lose some of their mechanical advantage. This is consistent with the findings of larger initial clockwise torsion in very early systole, as well as the decrease in Φ_{max} observed with cardiomyopathy. In addition, fiber-angle remodeling, which was not measured in this study, could also contribute to the torsion changes we observed. An alternative hypothesis is suggested by the anatomic studies of Torrent-Guasp and colleagues,[35] who found that ventricular muscle can be unwrapped into basal and apical loops. If the sequence of activation of muscle proceeds linearly along this band, the delayed Φ_{max} and loss of recoil during IVR may be explained by slowed activation of the apical loop. Further studies of the electrical activation of this band, however, must be done to support this theory. The present interpretation is consistent with findings that demonstrate an endocardial to epicardial activation wave.[36-38]

Second, transmural fiber activation is slowed during LV ischemia and TIC conditions, a finding attributed to fibrosis and remodeling of gap junctions in models of heart failure.[37,39,40] Slowed transmural conduction would leave the subendocardial fibers unopposed relative to subepicardial fibers for a longer period of time in early systole, allowing for a larger and longer initial clockwise twist, as seen in cardiomyopathic hearts in this study. The increase in Φ_{min} might contribute to a decrease in Φ_{max} because the positive torsional deformation attributed to the subepicardium must begin at a lower baseline after the delay. Delayed subepicardial activation caused by slowed transmural conduction, as reported by Delhass and coworkers,[37] might slightly prolong systolic contraction and contribute to the delay in the timing of Φ_{max}.

A third factor possibly contributing to the observed changes in torsion mechanics are the alterations in myocyte action potentials and intracellular calcium regulation associated with heart failure. TIC causes decreased amplitude and increased duration of the action potential.[41] TIC has also been linked to reduction in Ca^{2+} transients,[42] maximal Ca^{2+}-activated tension, and peak force generation.[43] Such decreased tension generation might reduce all torsional moments and contribute to the decrease in Φ_{max} in cardiomyopathic hearts. Similarly, pacing-induced cardiomyopathy results in prolongation of both the Ca^{2+} transient and isometric contraction.[43,44] As in the case of delayed epicardial activation, these changes might prolong systolic contraction, leading to the delay in reaching Φ_{max} and loss of early diastolic recoil.

Extracellular changes associated with TIC may also help explain the derangements in torsional dynamics. Loss of the orderly collagen latticework[45] has been linked to reduced force generation in TIC. Spinale and coworkers[30] found that activation of matrix metalloproteinases and degradation of the fibrillar collagen matrix is an early event in TIC. Such matrix degradation could lead to ventricular dilatation and loss of coordinated myocyte contractile performance. In addition, because the extracellular matrix stores potential energy that is thought to be released during early diastole,[25] its degradation and disarray may contribute to the loss of diastolic torsional recoil.

The present findings indicate that dilated cardiomyopathy induced by rapid pacing significantly perturbs normal

systolic and diastolic LV torsional mechanics. We speculate that decreased torsion may play a role in the pathophysiology of TIC as part of a positive feedback loop. The ventricle compensates for systolic dysfunction and decreased cardiac output by dilating as TIC evolves, thereby reducing the mechanical advantage of the subepicardial LV fibers relative to the subendocardial fibers and decreasing systolic torsion. The associated steeper transmural gradients of fiber strain and oxygen demand lead to further systolic dysfunction, thereby continuing the cycle.

Limitations

The present study used an ovine TIC model, and therefore caution must be exercised in extrapolating these results to human subjects. Other investigators, however, have demonstrated that TIC has a hemodynamic and neurohumoral profile similar to that of dilated cardiomyopathy seen clinically.[10,11]

Previous studies have measured twist, or the longitudinal gradient of torsional displacement, along the long axis of the ventricle.[46] Measurement of twist, however, assumes homogeneous deformation of an isotropic cylindrical ventricle, resulting in a linear relationship of torsion and distance along the long axis. Instead, the present analysis measured rotation of the apex relative to the base, which is similar to that seen in other studies.[22,24,47] Stuber and colleagues[24] found that measurements of longitudinal gradient of rotation deformation (twist) correlated well with those of apical torsion. To ascertain whether the findings in this study, namely a decrease and delay in Φ_{max} and a decline in early LV diastolic torsional recoil, might have been phenomena specific to the apex, the analysis was repeated by using the markers located in the equatorial LV plane, midway between the base and apex (ie, nos. 3, 10, and 13; Figure 1). The torsion measurements at this level corroborate those at the apical level, both during ejection and during IVR and early diastole. Specifically, Φ_{max} was decreased and delayed, with a loss of early diastolic recoil.

Calculations of angular displacement are directly affected by ventricular dilatation (ie, arc length = radius · Φ). Normalization of Φ_{max}, Φ_{min}, and $\Phi_{5\%}$ for changes in ventricular size, however, did not significantly change the differences found between the control and TIC conditions. Similarly, normalization to correct for the faster heart rate after development of cardiomyopathy did not alter the delay of $T_{\Phi maxEE}$ observed in the TIC group. In the presence of mitral regurgitation, which developed in the TIC animals, ES and end-ejection may become temporally dissociated[48]; however, when the timing of Φ_{max} was measured relative to ES, the same trends were observed, as reported above.

This protocol was only approved by the Research Animal Use Committee for 2 data-acquisition studies, baseline and after development of cardiomyopathy. Thus we can only speculate about the time course of changes in ventricular geometry, hemodynamics, and torsion. Further experiments are underway to examine the temporal relationship between alterations in torsion, ventricular remodeling, and functional decline. Finally, the mitral regurgitation seen in the cardiomyopathic conditions could have been, at least in part, responsible for the altered hemodynamics and torsion mechanics seen in TIC.

Implications and Inferences

The current wave of clinical surgical enthusiasm for the Surgical Anterior Ventricular Endocardial Restoration[8] procedure, as promulgated by the Reconstructive Endoventricular Surgery returning Torsion Original Radius Elliptical shape to the LV (RESTORE) group, purports to reapproximate normal LV shape, size, and fiber angles, thereby theoretically restoring normal LV torsion mechanics in patients with ischemic and nonischemic dilated cardiomyopathy.[9] The present study supports the hypothesis that dilated cardiomyopathy is associated with derangements of physiologic torsion dynamics, and we speculate that these alterations may contribute to a cycle of progressive ventricular functional decline. LV systolic torsion and diastolic recoil can be measured noninvasively with radiofrequency-tagging magnetic resonance imaging.[24] Further clinical studies are needed to clarify the role of torsion in the pathophysiology of human cardiomyopathy.

References

1. Greenbaum RA, Ho SY, Gibson DG, Becker AE, Anderson RH. Left ventricular fibre architecture in man. *Br Heart J.* 1981;45:248-63.
2. Spotnitz HM. Macro design, structure, and mechanics of the left ventricle. *J Thorac Cardiovasc Surg.* 2000;119:1053-77.
3. Ingels NB Jr, Daughters GT, Stinson EB, Alderman EL. Measurement of midwall myocardial dynamics in intact man by radiography of surgically implanted markers. *Circulation.* 1975;52:859-67.
4. Buchalter MB, Rademakers FE, Weiss JL, Rogers WJ, Weisfeldt ML, Shapiro EP. Rotational deformation of the canine left ventricle measured by magnetic resonance tagging: effects of catecholamines, ischaemia, and pacing. *Cardiovasc Res.* 1994;28:629-35.
5. Arts T, Reneman RS. Dynamics of left ventricular wall and mitral valve mechanics—a model study. *J Biomech.* 1989;22:261-71.
6. Beyar R, Sideman S. The dynamic twisting of the left ventricle: a computer study. *Ann Biomed Eng.* 1986;14:547-62.
7. Rademakers FE, Buchalter MB, Rogers WJ, Zerhouni EA, Weisfeldt ML, Weiss JL, et al. Dissociation between left ventricular untwisting and filling. Accentuation by catecholamines. *Circulation.* 1992;85:1572-81.
8. Athanasuleas CL, Stanley AW Jr, Buckberg GD, Dor V, DiDonato M, Blackstone EH. Surgical anterior ventricular endocardial restoration (SAVER) in the dilated remodeled ventricle after anterior myocardial infarction. RESTORE group. Reconstructive Endoventricular Surgery, returning Torsion Original Radius Elliptical Shape to the LV 1. *J Am Coll Cardiol.* 2001;37:1199-209.
9. Buckberg GD. Congestive heart failure: treat the disease, not the symptom—return to normalcy 7. *J Thorac Cardiovasc Surg.* 2001;121:628-37.
10. Patel HJ, Pilla JJ, Polidori DJ, Pusca SV, Plappert TA, Sutton MS, et al. Ten weeks of rapid ventricular pacing creates a long-term model of left ventricular dysfunction. *J Thorac Cardiovasc Surg.* 2000;119:834-41.

11. Armstrong PW, Stopps TP, Ford SE, de Bold AJ. Rapid ventricular pacing in the dog: pathophysiologic studies of heart failure. *Circulation.* 1986;74:1075-84.
12. Lai DT, Timek TA, Dagum P, Green GR, Glasson JR, Daughters GT, et al. The effects of ring annuloplasty on mitral leaflet geometry during acute left ventricular ischemia. *J Thorac Cardiovasc Surg.* 2000;120: 966-75.
13. Moon MR, DeAnda A Jr, Daughters GT, Ingels NB Jr, Miller DC. Experimental evaluation of different chordal preservation methods during mitral valve replacement. *Ann Thorac Surg.* 1994;58:931-43.
14. Taber LA, Yang M, Podszus WW. Mechanics of ventricular torsion. *J Biomech.* 1996;29:745-52.
15. Beyar R, Sideman S. Left ventricular mechanics related to the local distribution of oxygen demand throughout the wall. *Circ Res.* 1986; 58:664-77.
16. Arts T, Hunter WC, Douglas A, Muijtjens AM, Reneman RS. Description of the deformation of the left ventricle by a kinematic model. *J Biomech.* 1992;25:1119-27.
17. Ohayon J, Chadwick RS. Theoretical analysis of the effects of a radial activation wave and twisting motion on the mechanics of the left ventricle. *Biorheology.* 1988;25:435-47.
18. Beyar R, Sideman S. Effect of the twisting motion on the nonuniformities of transmyocardial fiber mechanics and energy demand—a theoretical study. *IEEE Trans Biomed Eng.* 1985;32:764-9.
19. Coleman HN III, Taylor RR, Pool PE, Whipple GH, Covell JW, Ross J Jr, et al. Congestive heart failure following chronic tachycardia. *Am Heart J.* 1971;81:790-8.
20. Spinale FG, Tanaka R, Crawford FA, Zile MR. Changes in myocardial blood flow during development of and recovery from tachycardia-induced cardiomyopathy. *Circulation.* 1992;85:717-29.
21. Yun KL, Miller DC. Torsional deformation of the left ventricle. *J Heart Valve Dis.* 1995;4(suppl 2):S214-20.
22. Kroeker CA, Tyberg JV, Beyar R. Effects of ischemia on left ventricular apex rotation. An experimental study in anesthetized dogs. *Circulation.* 1995;92:3539-48.
23. Bell SP, Nyland L, Tischler MD, McNabb M, Granzier H, LeWinter MM. Alterations in the determinants of diastolic suction during pacing tachycardia. *Circ Res.* 2000;87:235-40.
24. Stuber M, Scheidegger MB, Fischer SE, Nagel E, Steinemann F, Hess OM, et al. Alterations in the local myocardial motion pattern in patients suffering from pressure overload due to aortic stenosis. *Circulation.* 1999;100:361-8.
25. Beyar R, Yin FC, Hausknecht M, Weisfeldt ML, Kass DA. Dependence of left ventricular twist-radial shortening relations on cardiac cycle phase. *Am J Physiol.* 1989;257(suppl):H1119-26.
26. Yun KL, Niczyporuk MA, Daughters GT, Ingels NB Jr, Stinson EB, Alderman EL, et al. Alterations in left ventricular diastolic twist mechanics during acute human cardiac allograft rejection. *Circulation.* 1991;83:962-73.
27. Nagel E, Stuber M, Lakatos M, Scheidegger MB, Boesiger P, Hess OM. Cardiac rotation and relaxation after anterolateral myocardial infarction. *Coron Artery Dis.* 2000;11:261-7.
28. Dong SJ, Hees PS, Huang WM, Buffer SA Jr, Weiss JL, Shapiro EP. Independent effects of preload, afterload, and contractility on left ventricular torsion. *Am J Physiol.* 1999;277(suppl):H1053-60.
29. Hansen DE, Daughters GT, Alderman EL, Ingels NB, Stinson EB, Miller DC. Effect of volume loading, pressure loading, and inotropic stimulation on left ventricular torsion in humans. *Circulation.* 1991; 83:1315-26.
30. Spinale FG, Coker ML, Thomas CV, Walker JD, Mukherjee R, Hebbar L. Time-dependent changes in matrix metalloproteinase activity and expression during the progression of congestive heart failure: relation to ventricular and myocyte function. *Circ Res.* 1998;82: 482-95.
31. LeGrice IJ, Takayama Y, Holmes JW, Covell JW. Impaired subendocardial function in tachycardia-induced cardiac failure. *Am J Physiol.* 1995;268(suppl):H1788-94.
32. Spinale FG, Zellner JL, Johnson WS, Eble DM, Munyer PD. Cellular and extracellular remodeling with the development and recovery from tachycardia-induced cardiomyopathy: changes in fibrillar collagen, myocyte adhesion capacity and proteoglycans. *J Mol Cell Cardiol.* 1996;28:1591-608.
33. Chow E, Woodard JC, Farrar DJ. Rapid ventricular pacing in pigs: an experimental model of congestive heart failure. *Am J Physiol.* 1990; 258(suppl):H1603-5.
34. Ingels NB Jr, Hansen DE, Daughters GT, Stinson EB, Alderman EL, Miller DC. Relation between longitudinal, circumferential, and oblique shortening and torsional deformation in the left ventricle of the transplanted human heart. *Circ Res.* 1989;64:915-27.
35. Torrent-Guasp F, Ballester M, Buckberg GD, Carreras F, Flotats A, Carrio I, et al. Spatial orientation of the ventricular muscle band: physiologic contribution and surgical implications 1. *J Thorac Cardiovasc Surg.* 2001;122:389-92.
36. Durrer D, Dam Rv, Freud GE, Janse MJ, Meijler FL, Arzbaecher RC. Total excitation of the isolated human heart. *Circulation.* 1970;41: 899-912.
37. Delhaas T, Arts T, Prinzen FW, Reneman RS. Regional electrical activation and mechanical function in the partially ischemic left ventricle of dogs. *Am J Physiol.* 1996;271(suppl):H2411-20.
38. Shors SM, Sahakian AV, Sih HJ, Swiryn S. A method for determining high-resolution activation time delays in unipolar cardiac mapping 1. *IEEE Trans Biomed Eng.* 1996;43:1192-6.
39. De Mello WC. Cell coupling and impulse propagation in the failing heart. *J Cardiovasc Electrophysiol.* 1999;10:1409-20.
40. Arenal A, Villemaire C, Nattel S. Mechanism of selective epicardial activation delay during acute myocardial ischemia in dogs. *Circulation.* 1993;88:2381-8.
41. Mukherjee R, Hewett KW, Spinale FG. Myocyte electrophysiological properties following the development of supraventricular tachycardia-induced cardiomyopathy. *J Mol Cell Cardiol.* 1995;27:1333-48.
42. O'Rourke B, Kass DA, Tomaselli GF, Kaab S, Tunin R, Marban E. Mechanisms of altered excitation-contraction coupling in canine tachycardia-induced heart failure, I: experimental studies. *Circ Res.* 1999;84:562-70.
43. Perreault CL, Shannon RP, Komamura K, Vatner SF, Morgan JP. Abnormalities in intracellular calcium regulation and contractile function in myocardium from dogs with pacing-induced heart failure. *J Clin Invest.* 1992;89:932-8.
44. Winslow RL, Rice J, Jafri S, Marban E, O'Rourke B. Mechanisms of altered excitation-contraction coupling in canine tachycardia-induced heart failure, II: model studies. *Circ Res.* 1999;84:571-86.
45. Spinale FG, Tomita M, Zellner JL, Cook JC, Crawford FA, Zile MR. Collagen remodeling and changes in LV function during development and recovery from supraventricular tachycardia. *Am J Physiol.* 1991; 261(suppl):H308-18.
46. DeAnda A Jr, Komeda M, Nikolic SD, Daughters GT, Ingels NB, Miller DC. Left ventricular function, twist, and recoil after mitral valve replacement. *Circulation.* 1995;92(suppl 9):II458-66.
47. Moon MR, Ingels NB Jr, Daughters GT, Stinson EB, Hansen DE, Miller DC. Alterations in left ventricular twist mechanics with inotropic stimulation and volume loading in human subjects. *Circulation.* 1994;89:142-50.
48. Brickner ME, Starling MR. Dissociation of end systole from end ejection in patients with long-term mitral regurgitation. *Circulation.* 1990;81:1277-86.